PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The RECARDINA study protocol: diagnostic utility of ultra-abbreviated echocardiographic protocol for hand-held machines used by non-experts to detect rheumatic heart disease
AUTHORS	Francis, Joshua; Fairhurst, Helen; Whalley, Gillian; Kaethner, Alex; Ralph, A; Yan, Jennifer; Cush, James; Wade, Vicki; Monteiro, Andre; Remenyi, Bo

VERSION 1 – REVIEW

REVIEWER	Bruno Ramos Nascimento Hospital das Clínicas da Universidade Federal de Minas Gerais, Brazil.
REVIEW RETURNED	02-Mar-2020

GENERAL COMMENTS	At first, congraulations for an interesting protocol, addressing a topic of interest for global health. The utilization of simplified screening protocols for RHD has gained importance recently, especially in underserved areas, with the possibility of task-shifting to non-physicians. However, clinical outcomes of echocardiography-detected RHD are still under evaluation, as well as the protective effect of Pennicilin on this population. However, some points of the protocol need clarification prior to publication: 1) For accuracy estimates, a sample of normal exams should be randomly evaluated. Ideally, the authors should select a sample of individuals with negative Lumify studies performed by the non-physician and physician, to undergo a complete screening echo with a regular portable machine instead of a handheld. This would make accuracy data more reliable. 2) For the echo outcome, more than the differentiation between normal, borderline and definite RHD, the authors should consider evaluating the sensitivity (and negative predictive value) of non-experts to identify cases at higher risk for progression. Such re-classifications have been proposed by Beaton et al (Circulation, 2017): borderline + mild definite vs. moderate/severe definite, and by Nunes et al (Circulation Cardiovasc Imaging 2019), as a point-based score (>=10 points = high risk). Even without changing the original protocol, the evaluation of the hability of the simplified protocol to rule-in such cases would be informative, as progression over time is a key question for subclinical RHD. 3) The authors will initiate secondary prophylaxis for children with definite RHD diagnosed by echo. Please provide the background for this decision, as the effect of Penicillin in this population is uncertain and is still under investigation in the GOAL trial, in Uganda. Even the GOAL trial randomizes children with higher risk features for placebo vs. prophylaxis, per protocol. 4) For positive cases flagged as positive by the physician of non-

	physician during screening, the images of the full screening echocardiogram will be analyzed by a single expert? If so, maybe a random sample should be sent for a double-review, with a tie-breaker if doubts persist. Sometimes diagnosis of subtle abnormalities, especially in borderline cases, may be challenging and prone to imprecision. Ideally all positive cases should undergo this pathway, but it may not be feasible.

REVIEWER	Prof. Philippe Le Conte, MD, PhD Department of Emergency Medicine Nantes University Hospital Nantes, France
REVIEW RETURNED	01-Apr-2020

GENERAL COMMENTS	Thank you to give me the opportunity to review this interesting paper about a research protocol focused on rheumatic heart disease detection. The paper is well-written, The endpoints seems to be well-chosen and reasonable. I have no major comment. Few little modifications could enhance the overall quality: • consider adding study protocol in the title • please modify the figure 2 since the two presented algorithms seem identical

VERSION 1 – AUTHOR RESPONSE

Reviewer 1
1. For accuracy estimates, a sample of normal exams should be randomly evaluated.
Thank you for this suggestion. A selection of cases will undergo a complete screening echo. This has now been included on page 6.

2. For the echo outcome, more than the differentiation between normal, borderline and definite RHD, the authors should consider evaluating the sensitivity (and negative predictive value) of non-experts to identify cases at higher risk for progression.
Thank you for this suggestion. We will include this analysis and have indicated this on page 8.

3. The authors will initiate secondary prophylaxis for children with definite RHD diagnosed by echo. Please provide the background for this decision.
This approach is based on current Australian guidelines, which has been clarified on page 8.

4. For positive cases flagged as positive by the physician of non-physician during screening, the images of the full screening echocardiogram will be analyzed by a single expert? If so, maybe a random sample should be sent for a double-review, with a tie-breaker if doubts persist.
On page 7 we have clarified that all abnormal cases will be reviewed by a panel of three experts. In addition, experts will be encouraged to request a panel in cases that are deemed normal, if there are findings that could be seen in borderline or definite RHD.

Reviewer 2:
5. Consider adding study protocol in the title.
The words “study protocol” are included in the title.

6. Please modify the figure 2 since the two presented algorithms seem identical.
Figure 2 explains two different approaches to determining if a SPLASH echo, performed by a health

worker, warrants further investigation. The difference between the two is subtle, but involves off-site expert review of SPLASH images in approach 2, represented by a box. The rest of the flow of patients using this approach is the same as for approach 1.

VERSION 2 – REVIEW

REVIEWER	Bruno Ramos Nascimento Hospital das Clínicas da Universidade Federal de Minas Gerais
REVIEW RETURNED	02-May-2020

GENERAL COMMENTS	My main concerns, regarding the utilization of sub-groups for subclinical RHD (subdivisions of the definite category, and high-risk groups based on the prediction score by Nunes et al). have been met in this revision. It is important that such variables are primarily collected in the data-colection form or tool.